

In the Specification

Applicant presents replacement paragraphs below indicating the changes with insertions indicated by underlining and deletions indicated by strikeouts and/or double bracketing.

Please replace paragraph 2 on page 8, line 11 through page 9, line 5 with the amended paragraph as follows:

Plate lifters 102, 103, 104 and 105 all extend from carriage 106 and move in an X direction (as shown in Fig. 1) along with a carriage 106. Carriage 106 rides along X slides 108 in the X direction under the control of an X drive motor 126 and along Y slides 122 in the Y-direction under the control of a Y drive motor 124, to position plate lifters 102, 103, 104 and 105 at the desired location in the X and Y directions. Plate lifters 102, 103, 104 and 105 also move in the Z direction, as shown in Fig. 1, with respect to carriage 106, under the control of associated Z drive motors 118. In the configuration illustrated in Figs. 1 and 2, plate lifters 102 and 104 are moved in the Z direction to retrieve and return plates 12 to the stacker assemblies 20-26, and to lift plates 12 up to head assembly 500. In the configuration illustrated in Figs. 1 and 2, platelifter 103 is moved in the Z direction to raise the fill station to head assembly 500, as will be described, while plate lifter 105 is moved in the Z direction to raise wash station 250 to head assembly 500, as will be described. Movement in the Y direction allows adjustment of the position of plate lifters 102, 103, 104 and 105 with respect to stacker assemblies 20-26 and head assembly 500, and allows use of plate lifters 102 and 104 to separate plates 12 that are stuck together in stacker assemblies 20-26, as will be described. X and Y movement of the platelifters also allows system 10 to be programmed to cause head 600 to withdraw liquid from a plate which has a substantially larger number of wells than assembly 500 has tips 702, and to expel liquid into daughter plates that also have a substantially larger number of wells than assembly 500 has tips 702 (Fig. 16). By moving plates 12 with respect to head 600, liquid may be withdrawn from or expelled into different quadrants of a substantially larger plate 12. Finally, movement in the X and Y directions permits movement of ~~trays~~ plates 12 with respect to the tips 702 of assembly 500 to provide access to different locations within a well 11, and to wipe liquid from the tips 702 on the edge of a well 11 (Fig. 20). Substantially all of the X, Y and Z drive

motors and drive belts are preferably enclosed within a housing 14 for safety and aesthetic purposes.

Please replace paragraph 3 on page 9, lines 19-31 with the amended paragraph as follows:

Column 110 of each plate lifter independently moves in the Z direction (as shown in Fig. 1) with respect to carriage 106, along Z slides 116 (see Figs. 3 and 5). Columns 110 are driven in the Z direction by Z drive motors 118 and Z belts 120. Details of two exemplary couplings of Z drive motors 118 and belts 120 to associated plate lifters 102 and 104 are illustrated in Figs. 3 and 5. Fig. 3 illustrates one example with respect to plate lifter 104, while Fig. 5 illustrates another example with respect to plate lifter 102. Like numbers are used for like parts, where applicable. In Fig. 3, belt 120 extends between idler pulleys 115 and over drive pulley 117 which is mounted to Z drive motor 118. Belt 120 is affixed to column 110 by a bracket 113. In Fig. 5, drive pulley 117 is intermediate two idler pulleys 115 and additional idler pulleys 111 are disposed on either side of drive pulley 117. It is understood, of course, that other conventional couplings and drive systems may be used to control movement of plate lifters 102 and 104 in the Z-direction.

Please replace paragraphs 1 and 2 on page 10, lines 1-17 with the amended paragraphs as follows:

Carriage 106 with plate lifters 102, 103 104 and 105 typically is moved both forward and backward in the Y direction, as shown in Fig. 1, along associated Y slides 122 by Y drive motor 124 and belt ~~126~~ 130 (See Fig. 4). An exemplary embodiment of the coupling of Y drive motor 124 and belt ~~126~~ 130 to carriage 106 is illustrated in Fig. 4. Belt ~~126~~ 130 extends between pulley 121 mounted on motor 124, and pulley 123. Bracket 125 affixes belt ~~126~~ 130 to the underside of carriage 106. Y slides 122 ~~includes~~ include spaced limit sensors 119 which send a signal to processor 292 which in turn controls motor 124 for control of movement of carriage 106 in the Y direction. Pads 112 may be rapidly oscillated, for example, to separate a plate 12

from another plate 12 to which it is stuck in a stacker assembly or to adjust the position of pads 112 in the Y-direction as needed. It is understood of course that conventional couplings and systems may be used to drive and control movement of plate lifters 102, 103, 104 and 105 in the Y-direction and that separate Y drives could be used for each plate lifter 102, 103, 104 and 105.

Z slides 116, Z drive motor 118, Z belt 120, ~~Z slides 116~~ and pulleys 111, 115 and 117 for plate lifters 102, 103, 104 and 105 are all mounted on ~~carriage 106~~ assembly 100 and move with carriage 106 in the X and Y directions. Similarly, Y drive motor 124, Y drive belt ~~126~~ 130, pulleys 121 and 123 and Y slides 122 are also mounted on ~~carriage 106~~ assembly 100 and travel with carriage 106 in the X direction and Y directions.

Please replace paragraph 3 on page 12, lines 21-29 with the amended paragraph as follows:

The back wall 36 of each chimney 28 comprises at least one and preferably two slots 62 and 64, each having angled guide surfaces feeding into the slot. These slots 62 and 64 are designed to be in registration with associated buttons 66 and 68 mounted on rear mounts 30 which in turn are mounted on housing wall 71. Buttons 66 and 68 support chimney 28, and the provision of two buttons 66 and 68 provides proper ~~vertical~~ alignment of chimney 28. In a preferred embodiment, button 66 includes a compression spring which urges button 66 toward back wall 36 of chimney 28 to hold back wall 36 tightly against rear mount 30 and which facilitates insertion of button 66 into associated slot 62 by providing some play in the position of button 66.

Please replace paragraph 4 on page 13, line 30 through paragraph 1, line 8 on page 15, with the amended paragraphs as follows:

Base assembly 32 is permanently mounted onto housing wall 71. Base assembly 32 typically includes two arms 32A and 32B, the ends of which are spaced from one another to provide an opening that is an extension of the opening between doors 40 to allow a user to grasp and slide plates 12 within base assembly 32. Base assembly 32 includes a plurality, typically 4,

of movable pins or arms 85. These arms 85 are retractable either by a stepper motor or the like (not shown) or by solenoids 84 and 94, which are either electrically or pneumatically actuated, as shown in Fig. 9. Each arm 85 extends from an associated solenoid or motor toward the interior of base assembly 32. Typically, solenoids 84 and 94 are disposed in aligned, opposed, spaced relationship in base assembly 32 as shown in Fig. 9. Preferably, four such solenoids 84 and 94 are employed. Each arm 85 is biased toward the interior of base assembly 32 by a biasing member, such as ~~an expansion~~ a compression spring 86 which bears against a spring keeper 87. Solenoids 84 and 94 are slidably disposed on pins 97 which permit adjustment of the position of solenoids 84 and 94 toward and away from the center opening of base assembly 32 using a spring mounted adjustment screw 99 or the like. The spring on screw 99 urges the solenoid 84 and 94 toward the center opening. This feature allows base assembly 32 to accommodate plates 12 of different sizes. Solenoids 84 and 94 are actuated by processor 292 to withdraw the distal ends of arms 85 from within the interior of chimney 28 so that the distal ends of arms 85 do not project beyond ridges 57 and 58. This actuation allows an assembly to accept and dispense plates 12 through its lower end, as will be described. Each solenoid 84 and 94 includes an upper, sloped surface 93 which typically extends into the center opening beyond respective ridges 57 and 58 and which guides the plates 12 into position in the center of base assembly 32 and into engagement with arms 85. As is apparent, the position of a surface 93 on a solenoid is adjusted when the position of its associated solenoid 84 or 94 is adjusted.

Plates 12 are individually removed by a plate lifter 104 by first lifting the stack and then by retracting arms 85 of solenoids 84 and 94 as shown in Fig. 14 and thereafter by quickly lowering the stack, and with a predetermined timing, by releasing arms 85 once lip 13 of the lower plate 12 passes and before the lip 13 on the next plate 12 passes to allow springs 86 to return arms 85 to a an extended position where which allows lip 13 on the next plate 12 is grabbed to be supported by arms 85. When plates 12 are inserted from below, plate lifter 104 raises the stack off arms 85 first and then arms 85 are withdrawn until the new plate 12 is lifted above solenoids 84 and 94. Once a new plate 12 passes upwardly, arms 85 are released ~~and to~~ catch a lip 13 on lowest plate 12, as the stack is lowered, as shown in Fig. 13 to prevent plates 12 from falling out of the bottom of base assembly 32.

In a preferred embodiment, the distal end of each arm 85 extending into the interior of base assembly 32 is beveled, with beveled surface 90 facing downwardly. It is desirable to maintain beveled surface 90 in a downwardly-facing direction to facilitate receipt by assembly 32 of plates 12 from below, when chimney 28 is mounted in base assembly 32. The bevel on arms 85 also allows the arms to extend into the small spaces below a lip 13 on the next lowest plate 12 and above the top of the lowest plate 12 as the lowest plate 12 is removed by a plate lifter 102 or 104 to allow removal of just one plate 12 at a time. The bevel on arms 85 also allows a plate 12 being inserted from below to push arms 85 out of the way as the stack is being raised. Maintenance of beveled surface 90 in a downwardly facing direction is accomplished by preventing rotation of arms 85 in solenoids 84 and 94. Disposed between spring 86 and each solenoid housing is a flag 88 which is mounted to arm 85 by a set screw or the like and which travels in a channel 89 to prevent rotation of arm 85.

Please replace paragraphs 2-3 on page 16, lines 4-25 with the amended paragraphs as follows:

Simultaneously with the foregoing, flaps 74 are engaged by upstanding walls 91, as shown in Fig. 11, causing flaps 74 to pivot upwardly against the biasing effect of torsion spring 78 until flaps 74 are in a generally vertical position generally parallel to walls 34 as shown in Fig. 10 (in which stacker chimney 28 is fully seated within base assembly 32). While flaps 74 are being pivoted upwardly, the distal ends of arms 85 of solenoids 84 and 94 are engaging lip 13 on the lowest plate 12 within chimney 28, and raising the lowest plate 12, and all of the other plates 12 stacked on top thereof, upwardly with respect to chimney 28 and away from flaps 74 to allow flaps 74 to pivot upwardly into the position shown in Fig. 10. When fully pivoted, as shown in Fig. 10, flaps 74 reside fully within channels 72 in side walls 34 so that they are completely spaced away from any plates 12 disposed within chimney 28.

When a chimney 28 is removed from its associated base assembly 32, the reverse occurs. Namely, as chimney 28 is raised, flaps 74 are raised above upstanding walls 91, thus allowing springs 78 to pivot flaps 74 into their open or generally horizontal position in which flaps extend into the interior of chimney 28. At the same time, arms 85 of solenoids 84 and 94 move

downwardly with respect to chimney 28. Arms 85 of solenoids 84 and 94 pass down through the openings of slots 80, as shown in Fig. 11. At about the point where arms 85 of solenoids 84 and 94 are generally even with flaps 74, flaps 74 are already in their open position and thus engage lip 13 of lowest plate 12, to prevent plates 12 from passing through the bottom of chimney 28, as shown in Fig. 12. At this same time, buttons 66 and 68 pass downwardly and out of respective slots 62 and 64 to allow complete removal of chimney 28 from base assembly 32.

Please replace paragraphs 1 and 2 on page 17, line 1 through page 18, line 2 with the amended paragraphs as follows:

Housing 502 includes a top wall 506 and side walls 508. Disposed on the lower end of each side wall 508 is a block 510 with a plurality of slideways for accepting head 600 ~~and tray~~ 700, as will be described. Extending between block 510 and top wall 506 are a plurality, typically four, of guide shafts 512 which guide vertical movement of generally horizontal plate 514. Plate 514 is moved in a generally vertical direction, or in a direction perpendicular to plate 514 by at least one, and preferably two threaded shafts 516, each of which passes through a nut or other fixture 518 which is mounted on plate 514, and which has a correspondingly threaded interior channel through which associated shaft 516 passes in threaded engagement. The upper end of each shaft 516 is coupled to an associated pulley 520. A motor 522 such as a servo motor or stepper motor, typically mounted behind housing 502, includes a shaft 524 extending from the rotor which has a pulley 526 mounted thereon. A belt 528 extends about pulleys 520 and 526. In this manner, each shaft 516 is rotated in synchronization with the other by motor 522 to raise and lower plate 514 with respect to housing 502. It should be understood that motor 522 may be coupled to shafts 516 by other well known means such as by gears and a chain or the like. Multiple coupling means, or multiple motors may also be used, so long as the movement of both shafts 516 is synchronized.

In one embodiment, disposed on the outside surface of each side wall 508 is a side bracket 530. Each bracket 530 includes an upper wall 532 and a lower wall 534 which extends at generally right angles to upper wall 532 toward tray 700, and which is disposed below block 510. Upper wall 532 is mounted to block 510 by screws or other like fasteners 536 which travel

in elongated slots 538 of upper wall 532 to guide vertical movement of bracket 530 with respect to side walls 508 and block 510. Each bracket 530 is biased into a normally up position in which lower wall 534 is urged against the lower surface of tray 700 by a biasing mechanism, such as extension springs 540. While four springs 540 are disclosed for each bracket 530, either a fewer or greater number of springs 540 may be used depending upon the desired biasing force, and the power force of each spring. Moreover, while springs 540 are preferred, it is understood that other biasing mechanisms such as pneumatic or electrical cylinders or the like may be utilized. It is understood, of course, that the biasing mechanism for each bracket 530 should apply a substantially identical biasing force. Springs 540 extend between posts 542 mounted on side wall 508 and ledge 544 of each bracket 530, which typically extends horizontally or at right angles to side wall 532 and away from side wall 508.

Please replace paragraph 2 on page 21, lines 8-26 with the amended paragraph as follows:

As illustrated in Fig. 20, head 600 includes a plurality of fluid withdrawal mechanisms 650. The number of such mechanisms corresponds to the number of tips 702 in tray 700. Typical examples include an array of 96 or 384 mechanisms 650. The number of tips 702 may correspond to the number of wells 11 in a plate 12 to be pipetted, or the number of tips 702 may be some known fraction of the number of wells 11. Each mechanism 650 includes a piston tube 660 having a piston rod 652 which is securely affixed at an upper end to plate 602. One means of affixation could include, for example, a pair of nuts 654 and 656 which are threaded onto a correspondingly threaded end of piston rod 652. It should be understood that other means may be used to affix or mount an upper end of piston rod 652 to plate 602, including braising, riveting, welding, gluing and the like. A distal end of each piston rod 652 extends into an associated piston chamber 658 which is formed inside piston tube 660 that extends from plate 604 through plate 606. Typically, an O-ring seal or the like 662 seals the upper end of chamber 658 about rod 652 ~~to prevent air and dirt from entering the upper portion of chamber 658.~~ Disposed on a lower surface of plate 606 is an opening 670 associated with each piston tube 660 which is in fluid communication with the piston chamber 658 disposed within. Openings 670 are

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configured to be aligned with the center of an upper end 704 of tips 702, as will be described. No nozzles are required as in ~~the~~ some prior art systems to couple piston chamber 658 to tips 702.

Please replace paragraph 5 on page 22, line 28 through page 23, line 2, with the amended paragraph as follows:

In the embodiment of Fig. 16, disposed against the back wall of housing 502 is a stop 716 which limits the distance that tray 700 can be pushed into housing 502 and which is spaced from detents 714 a distance such that when tray 700 is in place on lower wall 534, one end is resting against stop 716, while the other end is in engagement with detents 714, prior to raising plate 514. Preferably, a microswitch ~~708~~ 221 is disposed adjacent stop 716 to provide a signal to processor 292 when tray 700 is in place within housing 502.

Please replace paragraph 2 on page 23, lines 5-21 with the amended paragraph as follows:

The operation of pipetting head assembly 500 to insert or withdraw tray 700 will now be described with reference to Figs. 16 and 16A. If tray 700 is already in place, motor 522 is activated to move belt 528 in a direction which causes plate 514 to move downwardly toward tray 700. As plate 514 moves downwardly, the lower edge thereof engages pegs 546, thereby pushing bracket 530 downwardly toward tray 700 against the upward bias of springs 540. In the embodiment of Fig. 16A, plate 514 engages plates 572. This downward movement of bracket 530 or clamp 574 lowers lower wall 534 or surfaces 575 away from block 510 and tray 700, thereby releasing the clamping pressure on side extensions 710. Once plate 514 is in a position to release tray 700, motor 522 is stopped. At this point, upper ends 704 of tips 702 are spaced from seal 672, and, in Fig. 16, detents 714 are spaced sufficiently far from the underside of lip 712 to allow manual withdrawal of tray 700 by grasping of handle 720. Thereafter, a new tray 700 with clean tips 702 is inserted until the back surface of tray 700 engages stop 716 and triggers microswitch ~~708~~ 221 in Fig. 16, or until the back surface of tray 700 engages surfaces

577 in Fig. 16A. At this point, motor 522 is activated to raise plate 514 until plate 514 is raised above pegs 546 in Fig. 16, or above plates 572 in Fig. 16A. Springs 540 or 578 raise wall 534 or clamp 574 so that side extensions 710 are again clamped.

Please replace paragraphs 1-2 on page 24, lines 1-28 with the amended paragraphs as follows:

Other optional features of this invention will now be described with particular reference to Figs. 1, 2, 18, 23 and 24. In one alternative embodiment, this invention includes a fill station 200 which is mounted on one of the plate lifters of plate handling assembly 100, such as plate lifter 103. Fill station 200 may be used in place of mother plates 12 to supply fluid to daughter plates 12. To be so employed, fill station 200 is positioned directly below pipetting head assembly 500 by movement of carriage 106, using X drive motor 126 and Y drive motor 124, as described. Tips 702 are configured to extend into tub 230 of fill station 200 to permit withdrawal of liquid disposed therein. In use, fill station 200 is raised by pad 112 along Z slides 116, a Z drive motor 118 and belt 120. Fill station 200 is disposed in the position shown in Fig. 23. A suitable liquid 220 is supplied to fill station 200 through tube 214 by pump 208 which is controlled by control 210. Tube 214 is coupled to connector 216 which conducts liquid 220 to fill station 200. Liquid 220 is introduced to pump through input tube 212. Fill station 200 is provided with a conventional level detector 218 which makes certain that the level of liquid 220 within fill station 200 is maintained at the desired level so that fill station 200 does not overflow, and so that the distal ends ~~221~~ 708 of tips 702 are disposed within liquid 220 below the upper surface thereof. Connector ~~220~~ 222 (Fig. 1) for level sensor 218 is disposed on an outer wall of fill station 200.

In another embodiment of this invention, a wash station 250 may be provided. Wash station 250 includes upper chamber 272, lower chamber 274 and cylinders 270. Wash station 250 sits on a pad 112 of one of the plate lifters such as plate lifter 105. In operation, wash station 250 is raised to the position shown in Fig. 24. Wash station 250 is utilized to clean tips 702 which are disposed in tray 700. Pump 254 brings a wash liquid into tube ~~251~~ 256 (Fig. 1) and conducts the liquid through tube 258 to a coupling 260 which introduces the wash liquid into

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wash station 250. Coupling 262 removes used wash liquid from wash station 250 and conducts the used liquid through tube 264 to a waste location. Couplings 260 and 262 may be disconnected if desired, for removal of wash station 250.